Docket No.: 212033US0 DIV

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF :

Mitsuyo NAGANO, et al. : ATTN: APPLICATION DIVISION

SERIAL NO: NEW APPLICATION :

FILED: HEREWITH :

FOR: ANTITHROMBOTIC AGENT AND ANTI-VON WILLEBRAND FACTOR MONOCLONAL ANTIBODY

PRELIMINARY AMENDMENT

ASSISTANT COMMISSIONER FOR PATENTS
WASHINGTON, D.C. 20231

SIR:

Prior to examination on the merits, please amend the above-identified application as follows:

IN THE SPECIFICATION

Please amend the specification as shown in the marked-up copy to read as follows:

Please insert the following paragraph on page 1, after line 2:

--CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a division of U.S. application serial number 09/299,016, filed April 26, 1999 (now allowed), which is a division of U.S. application serial number 08/836,982, filed June 27, 1997 (now U.S. patent No. 5.916,805), which is a 37 C.F.R. §1.371 continuation of PCT International Application PCT/JP95/02435, filed November 29, 1995.--

Please replace the paragraph bridging pages 6 and 7 with the following paragraph:

--Several antibodies against vWF, which inhibit the activity of vWF in vitro, have been hitherto obtained. However, many of them are inferior in reaction specificity, and almost all of them do not inhibit the botrocetin-dependent reaction, even though they inhibit the ristocetin-dependent reaction. As described above, it is considered that the GPIb-binding site on vWF induced by ristocetin is homologous to that induced by botrocetin. Therefore, the foregoing antibodies possibly recognize the binding site on vWF for ristocetin or botrocetin. Strictly speaking, it is possible to say that they do not inhibit the physiological activity of vWF, and hence they have low reaction specificities. In such circumstances, it has been reported that two antibodies, i.e., NMC-4 produced by Fujimura et al. (J. Nara Med. Assoc., vol. 36, p. 662, 1985) and RFF-VIIIRAG:1 produced by Tuddenham et al., inhibit in vitro the reaction depending on both of ristocetin and botrocetin (Blood, vol. 17, No. 1, p. 113, 1991).--

Page 23, lines 8-24, please replace the paragraph with the following paragraph:

--Thus hybridomas AJvW-1, AJvW-2, AJvW-3, and AJvW-4 have been obtained as demonstrated in Examples described later on. All of them have been deposited on August 24, 1994 in National Institute of Bioscience and Human Technology of Agency of Industrial Science and Technology of Ministry of International Trade and Industry (postal code: 305, 1-3 Higashi-1-chome, Tsukuba-shi, Ibaraki-ken, Japan) under deposition numbers of FERM P-14486, FERM P-14487, FERM P-14488, and FERM P-14489 respectively in this order, which have been transferred to international deposition based on the Budapest Treaty on September 29, 1995, and deposited under deposition numbers of FERM BP-5247, FERM BP-5248, FERM BP-5249, and FERM BP-5250 respectively in this order. Among the

hybridomas, AJvW-2 and AJvW-4 produce the first monoclonal antibody, and AJvW-1 and AJvW-3 produce the second monoclonal antibody.--

IN THE CLAIMS

Please cancel Claims 1-14.

Please add the following claims:

--15. (New) A monoclonal antibody having the following properties:

(a) the monoclonal antibody binds to human von Willebrand Factor; and

(b) the monoclonal antibody inhibits binding between a monoclonal antibody produced by hybridoma and human von Willebrand Factor, when the monoclonal antibody is allowed to co-exist with a monoclonal antibody produced by a hybridoma which is selected from the group consisting of FERM BP-5248 (AJvW-2) , FERM BP-5250 (AJvW-4) and a variant of any of them.

16. (New) The monoclonal antibody according to Claim 15, which is produced by a hybridoma formed by fusion between mouse myeloma cells and spleen cells of a mouse immunized with human von Willebrand factor.

17. (New) The monoclonal antibody according to Claim 15, wherein the hybridoma is FERM BP-5248 (AJvW-2).

18. (New) The monoclonal antibody according to Claim 15, wherein the hybridoma is a variant of FERM BP-5248 (AJvW-2).

19. (New) The monoclonal antibody according to Claim 15, wherein the hybridoma is FERM BP-5250 (AJvW-4).

20. (New) The monoclonal antibody according to Claim 15, wherein the hybridoma is a variant of FERM BP-5250 (AJvW-4).

21. (New) A pharmaceutical composition having antithrombotic efficacy comprising the monoclonal antibody defined in Claim 15 and a pharmaceutically acceptable carrier.--

REMARKS

Claims 15-21 are active in this application.

The specification has been amended to include reference to related applications and to correct minor typographical errors. Newly added Claims 15-21 are supported by the specification at pages 9-53 and by claims 1-14 as originally filed. No new matter was added to the application by virtue of the present amendment. Applicants submit that the application is now ready for examination on the merits.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.

Norman F. Oblon
Attorney of Record
Registration No. 24,618

James J. Kelly, Ph.D.
Registration No. 41,504

Tel: 703-413-3000
Fax: 703-413-2220
NFO:JK:VKS:ksh
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Docket No.: **212033US0 DIV**

Serial No.: **New Application**

Amendment Filed: **July 31, 2001**

IN THE SPECIFICATION

Please amend the specification as follows:

Please insert the following paragraph on page 1, after line 2:

--(New).--

Please replace the paragraph bridging pages 6 and 7 with the following paragraph:

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IN THE CLAIMS

--Claims 15-21 (New).--